

# Moderate Hypothermic Versus Normothermic Total Cardiopulmonary Bypass for Coronary Artery Surgery: A Retrospective Study

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## Abstract

A retrospective analysis of 200 patients who underwent coronary artery bypass surgery between 1987 and 1990 was performed to ascertain whether there was any difference in morbidity or mortality with normothermic versus moderate hypothermic perfusion. Total cardiopulmonary bypass was used in all patients. 100 patients (Group H) were perfused using moderate (28-32°C) hypothermia and the remaining 100 patients (Group N) were perfused at normothermia (37°C). Both groups were comparable for age, weight, BSA, and perfusion time (Group H-mean 64 years, 82 Kg., 1.92 m<sup>2</sup>, 94 minutes; Group N-mean 63 years, 82 Kg., 1.90 m<sup>2</sup>, 90 minutes). Mean perfusate temperature in Group H was 31°C, while the normothermic group was maintained at 37°C. Both groups were perfused to maintain a venous

oxygen saturation between 65-70 percent and arterial pressure between 60-70 mmHg. The cardiac index during bypass for Group H was lower ( $2.32 \pm .19$  L/m<sup>2</sup>/min) than Group N ( $2.55 \pm .11$  L/m<sup>2</sup>/min) ( $p < 0.001$ ). Mean arterial pressure for Group H was  $69 \pm 12.4$  mmHg and for Group N was  $63 \pm 7.8$  mmHg ( $p < 0.001$ ). Oxygen transfer for Group N ( $159 \pm 43$  cc/min) was higher than Group H ( $113 \pm 31$  cc/min) ( $p < .001$ ). Metabolic acidosis was not observed in either group. Group H required vasodilators while Group N required vasoconstriction to maintain pressures on total bypass between 60-70 mmHg. Six patients in Group H and 13 patients in Group N required blood transfusion during bypass to maintain a hematocrit above 20 percent.

## Introduction

Hypothermia, defined as a condition in which core temperature is less than 35°C, is a universally accepted modality for cardiac surgery to reduce oxygen and metabolic requirements.<sup>1</sup> Current recognized levels of hypothermia are mild (37-32°C), moderate (32-28°C), deep (28-18°C), and profound (18-0°C).<sup>2</sup>

Hypothermia in conjunction with cardiac surgery was in use as early as the 1950s. Bigelow and others published several studies stating that deep hypothermia allowed successful heart surgery employing circulatory arrest.<sup>3,4,5</sup> As a result of this pioneering work, hypothermia has become an established regimen for all types of cardiac operations.

Initially, there was a trend to use deep hypothermia for organ protection, because of the substantial reduction

in metabolic and oxygen requirements. This was particularly advantageous because earlier gas transfer devices had limited capabilities and could not meet the demand. With the advent of chemical cardioplegia, the major concern of protecting the myocardium was satisfied. As a result, reduction of total body temperature to this level did not seem as critical. However, moderate levels were still employed.

The use of normothermic total cardiopulmonary bypass for cardiac operations is not a widely reported practice. This institution has utilized this technique since 1986 for routine coronary bypass and valve procedures with good results. To confirm our clinical impression that normothermic perfusion is a safe modality, two hundred patients were retrospectively studied to compare several intraoperative perfusion parameters between normothermia and moderate hypothermia. The following is a report of our clinical experience.

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## Materials and Methods

Retrospective analysis of perfusion data from two hundred patients was carried out to compare the results of moderate hypothermic versus normothermic total cardiopulmonary bypass during coronary artery surgery. One hundred patients (Group H) were perfused at moderate hypothermia (28-32°C), while the other hundred patients (Group N) were perfused at normothermia (37°C). All surgery was performed by the same surgeon (AKS). Both groups were comparable for age, weight, BSA and number of distal anastomoses (Table 1). Data was collected for venous oxygen saturation, arterial blood pressure, blood flow, O<sub>2</sub> transfer, systemic vascular resistance, fluid volumes and heparin requirements during bypass.

**Table 1**  
**Comparative Data for 200 Patients**

	Group H (N = 100)		Group N (N = 100)	
	Mean ± SD	Range	Mean ± SD	Range
Age (years)	64 ± 9	39 - 86	62 ± 9	41 - 84
Weight (kg)	80 ± 14.7	47 - 120	81 ± 14.1	51 - 119
BSA (m <sup>2</sup> )	1.92 ± .21	1.45 - 2.42	1.90 ± .21	1.38 - 2.44
Distal Anastomoses	3	2 - 4	3	2 - 4

All patients received general endotracheal anesthesia for surgery after a standard pre-medication of lorazepam (1 mg) PO, morphine sulphate (0.05-0.1 mg/kg) and scopolamine (0.05 mg/kg) IM. Anesthesia was induced with fentanyl (50 mcg/kg) IV and pancuronium (0.15mg/kg), low dose enflurane (0.5-1.0 percent), and occasionally midazolam (0.02-0.07 mg/kg) as necessary.

Arterial pressure was monitored via the radial artery. Central venous and pulmonary artery pressures were monitored via a Swan-Ganz catheter.<sup>a</sup> A median sternotomy was performed. Cannulation for arterial return was via the ascending aorta and bicaval cannulation with occlusive tapes via the superior and inferior vena cava for venous drainage. Left ventricular

decompression was accomplished via the superior pulmonary vein.

The perfusion circuit components were: A Capiox<sup>b</sup> or Maxima<sup>c</sup> membrane oxygenator, Medtronic filtered cardiotomy reservoir<sup>c</sup>, Terumo venous reservoir bag<sup>b</sup>, Medtronic arterial filter<sup>c</sup>, Cobe-Stockert roller pump<sup>d</sup>, and Gish ancillary tubing and connectors<sup>e</sup>. The prime solution consisted of: 2 L Isolyte<sup>f</sup>, 500 ml hetastarch, 12.5 grams mannitol, 50 mEq sodium bicarbonate, and 5,000 u beef lung heparin. A CDI 200 blood gas monitor<sup>g</sup> was used to assist in management of acid-base balance and an Oxy-Sat SM 0100<sup>h</sup> was used to monitor venous oxygen saturation while on bypass. Cardioplegia delivery was via a Gish CPS-1000 system.<sup>e</sup>

Patients were systemically heparinized with an initial dose of 300 u/kg of beef lung heparin. Five minutes after the initial dose, an ACT was performed and, if needed, a supplemental dose of heparin was given to maintain an ACT of approximately 480 seconds. ACTs were measured using a Hemochron 800.<sup>i</sup> Anticoagulation was subsequently monitored every 30 minutes while on bypass.

Bypass was initiated and Group H patients were cooled to a perfusate temperature between 28-32°C with an average of 31°C. Group N patients were maintained at 37°C perfusate temperature. A left ventricular vent was inserted via the right pulmonary vein for decompression. Total bypass was accomplished with superior and inferior vena cava clamps. Perfusion parameters were recorded every 15 minutes. The aorta was cross-clamped and arrest was facilitated with an infusion of 1,000 ml of crystalloid cardioplegia into the root at a delivery temperature of 6°C. This solution consisted of: 27 mEq NaCl, 30 mEq KCl, and 3 mEq. MgSO<sub>4</sub> in 5 percent dextrose and water. The pH was 7.8 and osmolarity was 357 mOsm/L. Subsequent infusions were with 12°C. blood cardioplegia containing: 1 mg. nitroglycerin, 530 mg. CPD, 20 mEq. KCl and 360 mg THAM. No crystalloid was added to the blood cardioplegia. Arterial pressure during bypass was maintained between 60-70 mmHg. Alpha-stat management for acid-base balance was utilized for both groups. Isoflurane or phenylephrine were used when either a dilator or constrictor response was necessary. After each distal anastomosis was completed, blood cardioplegia was infused through the vein graft for distal myocardial protection, as well as in the aortic root for global protection. This procedure was repeated for all vessels except the mammary artery, when cardioplegia was infused only into the aortic root. A single crossclamp was used for proximal and distal anastomoses. Rewarming was instituted upon completion of all distal anastomoses for Group H. Proximal anastomoses were then completed. Just prior to removal of the aortic crossclamp, an infusion of 300 ml of warm blood with 12.5 grams of manni-

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- b) Terumo Corporation, Somerset, NJ 08873
- c) Medtronic, Incorporated, Anaheim, CA 92807
- d) Cobe Laboratories, Incorporated, Lakewood, CO 80215
- e) Gish Biomedical, Incorporated, Santa Ana, CA 92705
- f) Kendall McGaw Laboratories, Inc., Irvine, CA 92714
- g) Cardiovascular Devices, Incorporated, Irvine, CA 92714
- h) Bentley Laboratories Incorporated, Irvine, CA 92714
- i) International Technidyne Corp., Edison, NJ 08820

**Table 2**

**Perfusion Parameters: Normothermia vs. Moderate Hypothermia**

	Group H (N=100)		Group N (N=100)	
	Mean ± SD	Range	Mean ± SD	Range
Temperature (°C)	31.1 ± .83	28-32	37	Norange
Pump Time (min)	94.1 ± 24	60 - 220	90.7 ± 18 . 8	61 - 174
Clamp Time (min)	63.9 ± 14.1	40 - 124	65.8 ± 14	41 - 112
O <sub>2</sub> Transfer (cc/min)	113.6 ± 31	54 - 211	159.8 ± 34	71 - 262
Blood Flow Rate (l/m <sup>2</sup> /min)	2.32 ± .19	1.82 - 2.79	2.55 ± .11	2.16 - 2.97
SVR (dynes sec cm <sup>-5</sup> )	1270 ± 230	738 -1880	1011 ± 217	640 - 1764
Arterial Pressure (mmHg)	69 ± 12.4	40 - 90	63 ± 7	50 - 85
TCO <sub>2</sub> (mEq/l)	25.2 ± 1.43	21 - 30	26.1 ± 2	22 - 30
pH	7.41 ± .01	7.37 - 7.46	7.42 ± .02	7.36 - 7.52
Isolyte (ml)	1006 ± 630	200 - 3000	764 ± 427	200 - 2000
Hetastarch (ml)	603 ± 250	250 - 1500	538 ± 148	250- 1000
ACT (sec)	567 ± 93	379 - 870	537 ± 111	331 - 981
Add'l Heparin (units x 1000)	6.3 ± 3.6	3 - 15	11 ± 6.8	4 - 30

tol was given. Vena caval clamps were removed and partial bypass was initiated. In most cases, spontaneous heart action was resumed. Defibrillation was incorporated when necessary. When patients were hemodynamically stable, bypass was terminated.

Data was retrospectively collected from the perfusion records. Derived data was acquired using the following formulas:

$\text{Systemic Vascular Resistance} = \frac{\text{MAP} - \text{CVP}}{\text{Blood Flow Rate}} \times 79.9$
$\text{Oxygen Transfer} = \frac{(\text{Art Sat} - \text{Ven Sat}) \times 1.34 \times \text{HCT} / 3 \times \text{Blood Flow Rate}}{100}$
$\text{Cardiac Index} = \frac{\text{Blood Flow Rate}}{\text{BSA}}$

**Results**

Data on 200 patients is presented in Table 2. Oxygen transfer in Group N (160 cc/min) was greater than in Group H (114 CC/min) (p< 0.001). Systemic vascular resistance was greater in Group H (1270 dynes sec cm<sup>-5</sup>) than in Group N (1011 dynes sec cm<sup>-5</sup>) (p< 0.001). Blood flow rate for Group H was lower than for Group N ( 2.32 versus 2.55 l/m<sup>2</sup>/min.) (p< 0.001).

Group H required isoflurane and/or nitroprusside

and Group N needed phenylephrine to maintain a perfusion pressure between 60-70 mmHg. Additional muscle relaxants and narcotics were also used for the normothermic group. Perfusion pressure for Group H averaged 69 mmHg, and Group N averaged 63 mmHg (p< 0.001).

Crystalloid and colloid fluid requirements were greater for Group H (Isolyte - 1006 ml/hetastarch - 603 ml) than for Group N (Isolyte - 764 ml/hetastarch - 538 ml). Six patients in Group H received at least one 250 cc unit of red cells while Group N patients received at least one unit in 13 patients.

Perfusion times for both groups were comparable (Group H - 94 minutes versus Group N - 91 minutes). The same was true for clamp times (Group H - 64 minutes versus Group N - 66 minutes).

Arterial blood pH averaged 7.41 for Group H and 7.42 for Group N, while maintaining an arterial pCO<sub>2</sub> of at least 40 mmHg. TCO<sub>2</sub> was comparable for both groups ( Group N= 26 mEq/L - Group H= 25 mEq/L).

Activated clotting times were comparable in Group H (567 sec) and Group N (537 sec) during bypass. Heparin requirement during bypass was greater for Group N (11,000units) than in Group H ( 6,300 units) (p< 0.001).

There were two post-operative deaths in Group H and none in Group N.

## Discussion

Early cardiac surgery utilizing extracorporeal circulation had the inherent problem of temperature maintenance. The initial intention was not to produce and maintain hypothermia, but rather to prevent this situation from occurring. The problem of extracorporeal heat loss remained unresolved until the advent of heat exchange devices in the perfusion circuit. Once proficiency in preventing heat loss was achieved, the next logical progression was to intentionally induce hypothermia, allowing reduction in total body flow thereby reducing non-coronary collateral blood flow for better surgical visibility, and reduce the metabolic demands of the patient. This was of particular benefit because of the relatively inefficient gas transfer devices of the time.

Once the technique of surface and core induced hypothermia was perfected, this became the mainstay of patient protection during cardiac surgery. However, one evident result of this technique was ventricular fibrillation, causing increased myocardial oxygen demand. This problem was resolved by the use of cold chemical cardioplegia solutions.

The question now arises as to whether total body hypothermia with its inherent problems, namely coagulopathies, uneven distribution of flow and temperature gradients, etc., is necessary given the following current available techniques used at this institution.

- 1) adequate myocardial protection (cold chemical cardioplegia and topical cooling)
- 2) total bypass utilizing bi-caval cannulation with venae cavae occlusion (to prevent excess warming of the heart)
- 3) adequate gas transfer devices
- 4) surgeon's acceptance of cardiac indices of 2.5 l/m<sup>2</sup>/min or higher with possible concurrent increased non-coronary flow
- 5) aortic cross clamp times (up to two hours)

As evidenced by these results, it seems that normothermic perfusion for cardiac surgery is a viable alternative. There were, as expected, differences between the two groups. Oxygen transfer was significantly less in Group H versus Group N because of reduced oxygen/metabolic requirements and vasoconstriction. Systemic vascular resistance was higher in Group H. More crystalloid and colloid volume replacement was required during bypass for Group H than Group N, but did not appear to have any clinical significance. One indicator of adequate perfusion for all cases was venous saturation. Therefore, the blood flow rate for the normothermic group was higher due to higher flow requirements to maintain this criteria.

Blood was required for six patients in the hypother-

mic group and 13 patients in the normothermic group to maintain an hematocrit of at least 20 percent. This difference was due to lower pre-bypass hematocrits in those particular patients.

No metabolic acidosis occurred in either group during total cardiopulmonary bypass. One would expect a mild acidosis during this period for the normothermic group.<sup>6</sup> However, with current oxygenating devices that can deliver fully oxygenated blood at adequate flow rates, this situation is seldom observed.

Activated clotting time was comparable for both groups on bypass. However, Group N required an average of 4,700 units of additional heparin to maintain a target activated clotting time of 480 seconds. This additional heparin probably reflects the difference in rate of metabolism between the two groups. Group N had one oxygenator failure which required replacement. This was accomplished without any adverse effects to the patient.

This data indicates that patients can be safely maintained in a state of hemodynamic and metabolic normalcy during normothermic total cardiopulmonary bypass.

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